

### REMARKS

Applicants respectfully request reconsideration. Claims 1-20 and 27 were previously pending in this application. Claims 21-26 have been withdrawn by the Examiner as being drawn to a non-elected invention. Claims 11 and 17 have been amended. New claims 28-30 have been added. As a result, claims 1-20 and 27-30 are pending for examination with claim 1 being independent claim. Applicants note that although claim 27 was added in the response filed on June 14, 2004, the addition of this claim was not acknowledged in the Office Action dated August 24, 2004. No new matter has been added.

#### Rejections under 35 U.S.C. §112

Claims 11 and 17 have been rejected under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claims 11 and 17 have been amended to clarify the subject matter that is claimed. In claim 11, "effected" has been replaced with "performed," as suggested by the examiner. Subject matter has been deleted from claim 17, and new claims 28-30 now recite the deleted matter.

Accordingly, withdrawal of the rejection of claims 11 and 17 under 35 U.S.C. §112 is respectfully requested.

#### Rejections Under 35 U.S.C. §102

Claims 1, 6-12 and 18-20 have been rejected under 35 U.S.C. §102(b) as being anticipated by Mignotte et al., "Mitochondrial DNA-Binding Proteins that Bind Preferentially to Supercoiled Molecules Containing the D-Loop Region of *Xenopus Laevis* mtDNA", *Biochemical and Biophysical Research Communications*, November 30, 1983 (Mignotte). Mignotte discloses the detection of a DNA protein interaction wherein DNA is bound to a protein and filtered on a nitrocellulose filter. Applicants fail to see where Mignotte discloses each and every step of the claimed invention.

Mignotte fails to disclose a method for detecting insoluble amyloid-like fibrils or protein aggregates in a sample. Furthermore, Mignotte does not describe contacting a filter with material of a sample suspected to comprise said fibrils or aggregates. Mignotte describes the

detection of a radioactively labeled DNA bound to a DNA binding protein (DBP). However, applicants cannot find in Mignotte disclosure that describes detecting whether amyloid-like fibrils or protein aggregates are retained on said filter, as recited in claim 1.

Furthermore, contrary to the assertion made by the Patent Office, the nitrocellulose filters disclosed by Mignotte typically possess a high capacity to bind soluble proteins. Applicants fail to see where Mignotte discloses either a filter having a low capacity for protein absorption or a filter comprising cellulose acetate. Therefore, claims 6 and 7 are patentable over Mignotte for this additional reason. Withdrawal of the rejection is respectfully requested.

#### Rejections Under 35 U.S.C. §103

The Examiner rejected claims 2, 3 and 5 under 35 U.S.C. §103(a) as being unpatentable over Mignotte in view of Tateishi et al., "Removal of Causative Agent of Creutzfeldt-Jacob Disease Through Membrane Filtration Method," *Membrane* (1993) (Tateishi). As provided above, Mignotte fails to disclose a method for detecting insoluble amyloid-like fibrils or protein aggregates in a sample. Applicants fail to see how Tateishi cures this deficiency.

The Office Action states that it would have been obvious to capture and detect the protein aggregates indicative of human neurodegenerative disease in the teaching of Tateishi using the method as taught by Mignotte wherein protein aggregates retained on the filter are detected and measured using microscopy because both Tateishi and Mignotte teach methods to achieve isolation and detection of detergent or urea-insoluble protein aggregates using a filter membrane.

Applicants disagree and believe that Tateishi teaches away from combining the two references. For instance, Tateishi discloses that after treatment with the surfactant Sarkosyl, that the CJD aggregates are separated into small pieces and pass through the filter with the filtrate. (Tateishi, at p. 361, col. 2). Thus, the method of Tateishi does not disclose filtering a sample to capture detergent or urea insoluble amyloid fibrils or protein aggregates, as claimed, but instead allows CJD aggregates that have been treated with Sarkosyl to pass through the filter with the filtrate. Thus, one skilled in the art would be led to believe that these CJD aggregates cannot be filtered after treatment with a surfactant, and therefore, would not be motivated to combine the two disclosures.

Furthermore, if one were to combine the teachings of the two disclosures, the claimed invention would not result, because neither Tateishi nor Mignotte disclose capturing insoluble amyloid-like fibrils or protein aggregates on a filter and detecting whether said fibrils or aggregates are retained on said filter.

The Office Action also states that the presence of PrPCJD protein is detected immunohistochemically using a chemical reagent. Applicants believe that the disclosure pointed to in the Office Action (p. 359, col. 1) is directed to an assay for the detection of PrPCJD from mouse brains infected with CJD and is not used for the detection of fibrils or aggregates that are retained on a filter, as claimed. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 14 and 17 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mignotte in view of Tateishi and in further view of Stott et al., *Proc. Nat'l. Acad. Sci. USA* (1995) (Stott). Stott discloses the incorporation of glutamine repeats in proteins implicated with neurodegenerative diseases. As detailed above, neither Mignotte or Tateishi disclose all of the elements recited in independent claim 1, and Applicants fail to see where Stott cures this deficiency. Thus, claim 1 and any claims that depend from it are patentable over the combination of Mignotte, Tateishi and Stott. Withdrawal of the rejection is respectfully requested.


**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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